MILLENNIUM

Please type a plus sign (+) inside this box -> +

PTO/SB/08B (10-96) Approved for use through 10/31/99. OMB 0654-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of Information unless it contains a valid OMB control number.

<del></del>		<del></del>		Сот	plete if Known	
Substitute	for form 1449	B/PTO				
11.150			CLOCHDE	Application Number	10/052,005	
			SCLOSURE	Filing Date	January 17, 2002	
STAT	TEMEN	TRY A	PPLICANT	First Named Inventor	Chen, Zhijian J.	
JIA	. FIA:F:			Group Art Unit	1652	
	(1100.00	nany sheets a	s nacessarv)	Examiner Name	Patterson, Charles, L., Jr.	
Sheet	1	of	5	Attorney Docket Number	MPI96-031CP1DV1CPACN1M	

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include the name of the author (in CAPTIAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and-or country where published.	T²
M.	EA /	Amason, T. and Ellison, M.J., "Stress resistance in Saccharomyces cerevisiae is strongly correlated with assembly of a novel type of multiubiquitin chain", Molecular and Cell Biology, Volume 14, Number 12, pages 7876-7883 (1994)	
	A5	Auphan, N., et al., "Immunosuppression by Glucocorticoids: Inhibition of NF-kB Activity Through Induction of IkB Synthesis" Science, Volume 270, pages 286-290 (1995)	
	A6 /	Baeuerle, P. and Henkel, T., "Function and Activation of NF-kB in the Immune System", Annual Review of Immunology, Volume 12, pages 141-179 (1994)	
	A11 J	Blank, J., et al., "Molecular Cloning of Mitogen-activated Protein/ERK Kinase Kinases (MEKK) 2 and 3", The Journal of Biological Chemistry, Volume 271, Number 10, pages 5361-5368 (1996)	
	B1 √	Chen, P., et al., "Multiplie Ubiquitin-Conjugating Enzymes Participate in the In Vivo Degradation of the Yeast MATα2 Repressor", Cell, Volume 74, pages 357-369 (1993)	
	B4 ,	Chen, Z., et al., "A 25-Kilodalton Ubiquitin Camer Protein (E2) Catalyzes Multiubiquitin Chain Synthesis via Lysine 48 of Ubiquitin", The Journal of Biological Chemistry, Volume 265, Number 35, pages 21835-21842 (1990)	
	B5 <sub>J</sub>	Choi, K., et al., "Ste5 Tethers Multiple Protein Kinases in the MAP Kinase Cascade Required for Mating in S. cerevisiae", Cell, Volume 78, pages 499-512 (1994)	
	В7 Ј	Derijard, B., et al., "Independent Human MAP Kinase Signal Transduction Pathways Defined by MEK and MKK Isoforms" Science, Volume 267, pages 682-685 (1995)	
	В8 √	Derijard, B., et al., "JNK1: A Protein Kinase Stimulated by UV Light and Ha-RAS That Binds and Phosphorylates the c-Jun Activation Domain", Cell, Volume 76, pages 1025-1037 (1994)	
M	B11 J	DiDonato, J., et al., "Phosphorylation of lkBa Precedes but Is Not Sufficient for Its Dissociation from NF-kB", Molecular and Cellular Biology, Volume 15, Number 3, pages 1302-1311 (1995)	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

T

Received from < 617 551 8820 - at 9/17/03 1:19:53 PM [Eastern Daylight Time]

<sup>&</sup>lt;sup>1</sup>Unique citation design number. <sup>2</sup>Applicant is to place a check mark here is English language Translation is attached.

2

Sheet

Please type a plus sign (+) inside this box

13:24 FAX 617 551

PTO/SB/08B (10-96) Approved for use through 10/31/99. OMB 0654-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Complete if Known Substitute for form 1449B/PTO 10/052005 Application Numb r INFORMATION DISCLOSURE January 17, 2002 Filing Date STATEMENT BY APPLICANT Chen, Zhijian J. First Named Inventor Group Art Unit 1652 Patterson, Charles L., Jr. Examiner Name (use as many sheets as necessary) MPI96-031CP1DV1CPACN1M of 5 Attorney Docket Number

Cite No.1	Include the name of the author (in CAPTIAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and-or country where published.	T <sup>2</sup>
B13 /	Finco, T., et al., "Inducible phosphorlation of IkBa is not sufficient for its dissociation from NF-kB and is inhibited by protease inhibitors", Proceedings of the National Academy of Sciences USA, Volume 91, pages 11884-11888 (1994)	
B15 /	Finco, T., et al., "Mechanistic Aspects of NF-kB Regulation: The Emerging Role of Phosphorylation and Proteolysis", Immunity, Volume 3, pages 263-272 (1995)	
B16 j	Francis, S. and Corbin, D., "Structure and Function of Cyclic Nucleotide-Dependent Protein Kinases" Annual Review of Physiology, Volume 56, pages 237-272 (1994)	
B18 J	Goldberg, A., "Functions of the Proteasome: The Lysis at the End of the Tunnel", Science, Volume 268, pages 522-523 (1995)	
Č1 j	Gupta, S., et al., "Transcription Factor ATF2 Regulation by the JNK Signal Transduction Pathway", Science, Volume 267, pages 389-393 (1995)	
C2 J	Haskill, S., et al., "Characterization of an Immediate-Early Gene Induced in Adherent Monocytes That Encodes IkB-like Activity", Cell, Volume 65, pages 1281-1289 (1991)	
C4 /	Hershko, A. and Heller, H., "Occurrence of a Polyubiquitin Structure in Ubiquitin-Protein Conjugates", Biochemical and Biophysical Research Communications, Volume 128, Number 3, pages 1079-1086 (1985)	
C6 √	Hibi, M., et al., "Identification of an oncoprotein- and UV-responsive protein kinase that binds and potentiates the c-Jun activation domain" Genes and Development, Volume 7, pages 2135-2148 (1993)	
C7 /	Higgins, K., et al., "Antisense inhibition of the p65 subunit of NF-kB blocks tumorigenicity and causes tumor regression", Proceedings of the National Academy of Sciences USA, Volume 90, pages 9901-9905 (1993)	
	No.1   B13 /     B15 /     B16 /	No.   City and-or country where published.   Finco, T., et al., "Inducible phosphorlation of IkBa is not sufficient for its dissociation from NF-kB and is inhibited by protease inhibitors", Proceedings of the National Academy of Sciences USA, Volume 91, pages 11884-11888 (1994)

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

<sup>&</sup>lt;sup>1</sup>Unique citation design number. <sup>2</sup>Applicant is to place a check mark here is English language Translation is attached.

Please type a plus sign (+) inside this box ->

PTO/SB/08B (10-96) Approved for use through 10/31/99. OMB 0654-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of Information unless it contains a valid OMB control number.

Substitute	for form 1449B	/PTO		Complete If Known		
		או סוכ	CLOCUDE	Application Number	10/052005	
			CLOSURE	Filing Date	January 17, 2002	
STA	TEMENT	L BY A	PPLICANT	First Named Inventor	Chen, Zhijian J.	
				Group Art Unit	1652	
	lusa as m	any sheets as	necessarv)	Examiner Name	Patterson, Charles L., Jr.	
Sheet	3	of	5	Attorney Docket Number	MPI98-031CP1DV1CPACN1M	

<u>-</u>		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include the name of the author (in CAPTIAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and-or country where published.	T <sup>2</sup>
M	C8 /	Hirano, M., et al., "MEK Kinase Is involved in Tumor Necrosis Factor α-Induced NF-kB Activation and Degradation of IkB-α", The Journal of Biological Chemistry, Volume 217, Number 22, pages 13234-13238 (1996)	
	C11 J	Lange-Carter, C.A., et al., "A Divergence in the MAP Kinase Regulatory Network Defined by MEK Kinase and Raf", Science, Volume 260, pages 315-319 (1993)	
	C13 /	Lln, YC., et al., "Activation of NF-kB requires proteolysis of the inhibitor IkB-a: Signal-induced phosphorylation of IkB- a alone does not release active NF-kB", Proceedings of the National Academy of Sciences USA, Volume 92, pages 552-556 (1995)	
-	C15	Mellits, K.H., et al., "Proteolytic degradation of MAD3 (IkB α) and enhanced processing of the NF-kB precursor p105 are obligatory steps in the activation of NF-kB", Nucleic Acids Research, Volume 21, Number 22, pages 5059-5066 (1993)	
	C16	Miyomoto, S., et al., 'Tumor necrosis factor α-induced phosphorylation of IkB α is a signal for its degradation but not dissociation from NF-kB", Proceedings of the National Academy of Sciences USA, Volume 91, pages 12740-12744 (1994)	
	D5	Read, M.A., et al., "The Proteasome Pathway is Required for Cytokine-Induced Endothelial-Leukocyte Adhesion Molecule Expression", Immunity, Volume 2, pages 493-506 (1995)	
	D10	Siebenilst, U., et al., "Structure, Regulation and Function of NF-kB", Annual Review of Cell Biology, Volume 10, pages 405-455 (1994)	
	D12 /	Thanos, D. and Maniatis, T., "NF-kB: A Lesson in Family Values", Cell, Volume 80, pages 529-532 (1995)	
CI	D13 /	Thevenin, C., et al., "Induction of Nuclear Factor-kB and the Human Immunodefiency Virus Long Terminal Repeat by Okadaic Acid, a Specific Inhibitor of Phosphatases 1 and 2A", New Biologist, Volume 2, Number 9, pages 793-800 (1990)	

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the Individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231.



<sup>&</sup>lt;sup>1</sup>Unique citation design number. <sup>2</sup>Applicant is to place a check mark here is English language Translation is attached.



Please type a plus sign (+) inside this box -> | +

PTO/SB/08B (10-96)
Approved for use through 10/31/99. OMB 0654-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO			Complete if Known		
			Application Number	10/052005	
RMATION	צוט ו	CLUSURE		January 17, 2002	
EMENT	$\nabla \Delta F$	PLICANT		Chen, Zhijian J.	
STATEMENT OF ALL FIGURE				1652	
funa na manu	hoote as	nocoecanyl		Patterson, Charles L., Jr.	
(USE AS THAIRY S		5		MPI98-031CP1DV1CPACN1M	
	RMATION EMENT E	RMATION DIS EMENT BY AF	RMATION DISCLOSURE EMENT BY APPLICANT (use as many sheets as necessary)	PRINT BY APPLICANT  (use as many sheets as necessary)  Application Number Filing Date First Named Inventor Group Art Unit Examiner Name	

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	1
Examiner	Cite No.1	Include the name of the author (in CAPTIAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and-or country where published.	T
AN	D15	Traenckner, E.B., et al., "Phosphorylatin of Human IkB-α on Serines 32 and 36 Controls IkB-α Protealysis and NF-kB Activation in Response to Diverse Stimuli", The EMBO Journal, Volume 14, Number 12, pages 2876-2883 (1995)	
	E3 /	Yang, YL., et al., "Deficient signaling in mice devoid of double-stranded RNA-dependent protein kinase", The EMBO Journal, Volume 14, Number 24, pages 6095-6106 (1995)	
	F1 J	Xu, S., et al., "Cloning of rat MEK kinase 1 cDNA reveals an endogenous membrane-associated 195-kDa protein with a large regulatory domain", Proceedings of the National Academy of Sciences USA, Volume 93, pages 5291-5295 (1996)	
	F2 /	Khoshnan, A., et al., "The Physical Association of Protein Kinase C0 with a Lipid Raft-Associated Inhibitor of kB Factor Kinase (IKK) Complex Plays a Role in the Activation of the NF-kB Cascade by TCR and CD28 <sup>1</sup> ", The Journal of Immunology, Volume 165, pages 6933-6940 (2000)	
	F3 /	DiDonato, J.A., et al., "A Cytokine-responsive IkB kinase that Activates the Transcription Factor NF-kB", Nature, Volume 388, pages 548-554 (August 1997)	
	F4 /	Miller, B.S. and Zandi, E., "Complete Reconstitution of Human IkB Kinase (IKK) Complex in Yeast", The Journal of Biological Chemistry, Volume 276, Number 39, pages 36320-36326 (September 28, 2001)	ľ
	F5 /	Fu, DX., et al., "Human T-lymphotropic Virus Type I Tax Activates I-kB Kinase by Inhibiting I-kB Kinase-associated Serine/Threonine Protein Phosphatase 2A", The Journal of Biological Chemistry, Volume 278, Number 3, pages 1487-1493 (January 17, 2003)	
	F6 v	Storz, P. and Toker, A., "Protein kinase D mediates a stress-induced NF-kB Activation and Survival Pathway", The EMBO Journal, Volume 22, Number 1, pages 109-120 (2003)	
	F7 /	Yang, J., et al., "The Essential Role of MEKK3 in TNF-induced NF-kB Activation", Nature Immunology, Volume 2, Number 7, pages 620-624 (July 2000)	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the Individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.

<sup>&</sup>lt;sup>1</sup>Unique citation design number. <sup>2</sup>Applicant is to place a check mark here is English language Translation is attached.

Please type a plus sign (+) Inside this box -> +

PTO/SB/08B (10-96) Approved for use through 10/31/99. OMB 0654-0031

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute	for form 1449	в/РТО		Complete If Known		
INICO		ON DIG	CI OCLIDE	Applicati n Number	10/052005	
			SCLOSURE	Filing Date	January 17, 2002	
STA	TEMEN	T BY A	PPLICANT	First Named Inventor	Chen, Zhijian J.	
0175			2.0	Group Art Unit	1652	
	luse as n	nany sheets a	s necessary)	Examiner Name	Patterson, Charles L., Jr.	
Sheet	5	of	5	Attorney Docket Number	MPI96-031CP1DV1CPACN1M	

		OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No.1	Include the name of the author (in CAPTIAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and-or country where published.	T <sup>2</sup>
M	F8 /	Zhao, Q. and Lee, F.S., "Mitogen-activated Protein Kinase/ERK Kinase Kinases 2 and 3 Activate Nuclear Factor-kB through IkB Kinase-a and IkB Kinase-B", The Journal of Biological Chemistry, Volume 274, Number 13, pages 8355-8358 (March 26, 1999)	
1	F9 /	Tojima, Y., et al., "NAK is an IkB kinase-activating kinase", Nature, Volume 404, pages 778-782 (April 13, 2000)	
	F10 /	Wang, C., et al., "TAK1 is a Ubiquitin-dependent kinase of MKK and IKK", Nature, Volume 412, pages 346-351 (July 19, 2001)	
	F11	Regnier, C.H., et al., "Identification and Characterization of an IkB Kinase", Cell, Volume 90, pages 373-383 (July 25, 1997)	
	F12 /	Connelly, M.A. and Marcu, K.B., "CHUK, A New Member of the Helix-loop-helix and Leucine Zipper Families of Interacting Proteins, Contains a Serine-Threonine Kinase Catalytic Domain", Cellular and Molecular Biology Research, Volume 41, Number 6, pages 537-549 (1995)	

·	Λ <i>l</i> / /	
Examiner	01/4///	Date 0/0/
Signature	1 Manuer	Considered /////
<u> </u>	717	

<sup>\*</sup>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>&</sup>lt;sup>1</sup>Unique citation design number. <sup>2</sup>Applicant is to place a check mark here is English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, D.C. 20231.